

CLAIMS

1. A peptide which enhances the ability of a drug to kill cells, characterized in that the
5 peptide consists essentially of the N2 sequence of the RasGAP protein, a fragment thereof, or
a variant thereof, which enhances said ability selectively in cancer cells.
2. The peptide of claim 1, characterized in that the fragment of the N2 sequence of the
RasGAP protein comprises the amino acid sequence of the SH3 domain of the N2 sequence, a
10 part thereof, or a variant thereof.
3. The peptide of claim 2, characterized in that the part of the SH3 domain, or the variant
thereof, contains less than or equal to 70 amino acids of the amino acid sequence of the SH3
domain.
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4. The peptide of claim 2, characterized in that the part of the SH3 domain consists in the
amino acid sequences encoded by the DNA sequences SEQ ID No.1, SEQ ID No.2, SEQ ID
No.3 or SEQ ID No.4.
- 20 5. The peptide of claim 1-4, characterized in that the peptide is conjugated to an agent
which increases the accumulation of said peptide in a cell.
6. The peptide of claim 5, characterized in that the agent is a cell membrane permeable
carrier.
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7. The peptide of claim 6, characterized in that the cell membrane permeable carrier is a
peptide.
8. The peptide of claim 7, characterized in that the cell membrane permeable carrier
30 peptide is an arginine rich peptide which is selected from the group comprising the HIV-TAT
48-57 peptide, the FHV-coat 35-49 peptide, the HTLV-II Rex 4-16 peptide and the BMV gag 7-25
peptide.

9. The peptide of claim 8, characterized in that the arginine rich peptide is the HIV-TAT
48-57 peptide

10. The peptide of claims 1 to 9, characterized in that the drug is a genotoxin.

11. The peptide of claim 10, characterized in that the genotoxin is selected from the group
comprising cisplatin, mitoxantrone and adriamycin.

12. An isolated and purified nucleic acid sequence comprising a nucleotide sequence
encoding the peptide of claims 1-4.

13. The nucleic acid sequence of claim 12 further comprising a nucleotide sequence
encoding a cell membrane permeable carrier peptide.

14. An expression vector comprising at least one copy of the isolated and purified nucleic
acid sequence of claim 12 or 13.

15. A prokaryotic or eukaryotic host cell containing the peptide of claims 1 to 4, the
isolated and purified nucleic acid sequence of claim 12 or 13 or the expression vector of claim

14.

16. A pharmaceutical composition comprising as an active substance a pharmaceutically
effective amount of at least one peptide of claims 1-9 optionally in combination with
pharmaceutically acceptable carriers, diluents and adjuvants.

17. The pharmaceutical composition of claim 16 for the treatment or prevention of cancer.

18. The use of the pharmaceutical composition of claim 16, for the preparation of a
medicament for the treatment or prevention of cancer.

19. Use according to claim 18, characterized in that the cancer is selected from the group
consisting of carcinoma, lymphoma, blastoma, sarcoma, liposarcoma, neuroendocrine tumor,

mesothelioma, schwannoma, meningioma, adenocarcinoma, melanoma, leukemia, lymphoid malignancy, squamous cell cancer, epithelial squamous cell cancer, lung cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, testicular cancer, esophageal cancer, a tumor of the biliary tract, and head and neck cancer.

20. The use according to claim 19, characterized in that the cancer is mesothelioma, testicular cancer or pancreatic cancer.

21. A method of treating or preventing cancer selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, liposarcoma, neuroendocrine tumor, mesothelioma, schwannoma, meningioma, adenocarcinoma, melanoma, leukemia, lymphoid malignancy, squamous cell cancer, epithelial squamous cell cancer, lung cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, testicular cancer, esophageal cancer, a tumor of the biliary tract, and head and neck cancer, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 16 to a subject in need thereof.

22. The method of claim 21, characterized in that the cancer is mesothelioma, testicular cancer or pancreatic cancer.

23. A method for enhancing apoptosis selectively in a cancer cell, comprising contacting a cancer cell with at least one peptide of claims 1-11 and a drug.

24. The method of claim 23, characterized in that the drug is a genotoxin.

25. The method of claim 24, characterized in that the genotoxin is selected from the group
5 comprising cisplatin, mitoxantrone, adriamycin.

26. A method for selectively killing cancer cells comprising contacting a cancer cell with
at least one peptide of claims 1-11 and a drug.

10 27. The method of claim 26, characterized in that the the drug is a genotoxin.

28. Use of the peptide of claims 1-11 for enhancing the ability of a genotoxin to kill cells
selectively in cancer cells.

15 29. A kit for treating or preventing cancer in a subject, said kit comprising at least one
peptide of claims 1-11 optionally with reagents and/or instructions for use.

30. The kit of claim 29, further comprising a separate pharmaceutical dosage form
comprising an additional anti-cancer agent selected from the group consisting of drugs, anti-
20 epidermal growth factor receptors antibodies, radioimmunotherapeutic agents, and
combinations thereof.

31. The peptide according to claims 1 to 9, characterized by the general sequence:

25 WXWVTXXRTX

wherein X is an amino acid residue.